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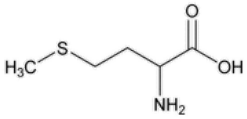
Racemethionine



$C_5H_{11}NO_2S$ 149.21

Methionine, DL-;

DL-2-Amino-4-(methylthio)-butyric acid CAS RN®: 59-51-8.

DEFINITION

Racemethionine contains NLT 99.0% and NMT 101.0% of $C_5H_{11}NO_2S$, as DL-methionine, calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: Dry the substances at 105°.

Acceptance criteria: Meets the requirements

• **B.** The principal spot from *Sample solution B* is similar in size, color, and position to the principal spot from *Standard solution A*, as obtained in the test for *Organic Impurities, Related Substances.*

• **C. Optical Rotation, *Angular Rotation*⟨781A⟩**

Sample: 50 mg/mL in 1 M hydrochloric acid

Acceptance criteria: −0.05° to +0.05°

• **D. Procedure**

Analysis: Dissolve 0.1 g of Racemethionine and 0.1 g of glycine in 4.5 mL of dilute sodium hydroxide solution (85 mg/mL). Add 1 mL of sodium nitroferricyanide solution (25 mg/mL). Heat to 40° for 10 min. Allow to cool, and add 2 mL of a mixture of hydrochloric acid and phosphoric acid (90:10).

Acceptance criteria: A deep red color develops.

ASSAY

• **Procedure**

Sample: 140 mg of Racemethionine

Analysis: Dissolve the *Sample* in a mixture of 3 mL of formic acid and 50 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary corrections (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 14.92 mg of $C_5H_{11}NO_2S$.

Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES

Inorganic Impurities

• **Residue on Ignition ⟨281⟩:** NMT 0.1%, determined on 1.0 g

• **Chloride and Sulfate, *Chloride*⟨221⟩:** [Note—Prepare the *Sample solution* and the *Standard solution* at the same time.]

Chloride standard solution (5 ppm Cl): 0.824 mg/mL of NaCl. Just before use, dilute 1 mL of this solution with water to 100 mL.

Standard solution: To 10 mL of *Chloride standard solution* add 10 mL of 0.1 N silver nitrate and 25 mL of water, and mix.

Sample solution: Dissolve 0.25 g in 35 mL of water. Add 5 mL of dilute nitric acid and 10 mL of 0.1 N silver nitrate. Allow to stand protected from light for 5 min.

Analysis: Examine the *Sample solution* and *Standard solution* laterally against a black background.

Acceptance criteria: Any opalescence in the *Sample solution* is not more intense than that in the *Standard solution* (200 ppm).

- **Chloride and Sulfate, *Sulfate*⟨221⟩:** [Note—Prepare the *Sample solution* and the *Control solution* at the same time.]

Barium chloride solution: 250 mg/mL

Sulfate standard solution (10 ppm SO_4): 1.81 mg/mL of potassium sulfate in 30% alcohol (v/v). Just before use, dilute 1 mL of this solution with 30% alcohol (v/v) to 100 mL.

Standard solution: Mix 3 mL of the *Barium chloride solution* and 4.5 mL of the *Sulfate standard solution*, and allow to stand for 1 min.

Sample stock solution: 50.0 mg/mL, heated to 60°. Cool to 10°, and filter.

Sample solution: To 2.5 mL of the *Standard solution* add 15 mL of the *Sample stock solution* and 0.5 mL of 5 N acetic acid.

Control solution: To 2.5 mL of the *Standard solution* add 15 mL of the *Sulfate standard solution* and 0.5 mL of 5 N acetic acid.

Analysis

Samples: *Sample solution* and *Control solution*

Acceptance criteria: After 5 min, any opalescence in the *Sample solution* is not more intense than that in the *Control solution* (200 ppm).

- **Limit of Iron**

Standard stock solution (125 ppm): Dissolve 1.727 g of ferric ammonium sulfate [$FeNH_4(SO_4)_2 \cdot 12H_2O$] in water. Add 50 mL of 10% hydrochloric acid, dilute with water to 1000 mL, and mix. Dilute 1 mL of this solution with water to 40 mL. Pipet 5 mL of this solution into a 200-mL volumetric flask, dilute with water to volume, and mix.

Standard solution: Transfer 2 mL of the *Standard stock solution* to a 25-mL volumetric flask. Add 5 mL of 16% hydrochloric acid, 50 mg of ammonium persulfate, and 3 mL of 30% ammonium thiocyanate, and dilute with water to volume.

Sample solution: Transfer 1 g of Racemethionine to a 25-mL volumetric flask. Add 5 mL of 16% hydrochloric acid, and dissolve. Add 50 mg of ammonium persulfate and 3 mL of 30% ammonium thiocyanate, and dilute with water to volume.

Blank: Transfer 5 mL of 16% hydrochloric acid to a 25-mL volumetric flask. Add 50 mg of ammonium persulfate and 3 mL of 30% ammonium thiocyanate, and dilute with water to volume.

Spectrometric conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 475 nm

Cell: 1 cm

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Without delay, concomitantly determine the absorbances of each sample, correcting for the *Blank*.

Acceptance criteria: The absorbance of the *Sample solution* is NMT that of the *Standard solution* (NMT 10 ppm).

- **Limit of Ammonium**

Standard solution A: 0.297 mg/mL of USP Ammonium Chloride RS. This solution contains 0.1 mg/mL or 100 ppm of NH_4^+.

Standard solution B: 0.297 µg/mL of USP Ammonium Chloride RS. This solution contains 0.1 µg/mL or 0.1 ppm of NH_4^+.

Standard solution C: 2.97 µg/mL of USP Ammonium Chloride RS. This solution contains 1.0 µg/mL or 1 ppm of NH_4^+.

Standard solution D: 29.7 µg/mL of USP Ammonium Chloride RS. This solution contains 10 µg/mL or 10 ppm of NH_4^+.

Sample solution: 10 mg/mL of Racemethionine

Electrode system: Use an ammonia-specific, ion-indicating electrode connected to a pH meter capable of measuring potentials (see *pH* ⟨791⟩).

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, and *Sample solution*

Add 100 mL of water to a 150-mL beaker, place the electrode in the beaker, stir, and measure the potential. Add 1 mL of 10 N sodium hydroxide. Stir, and measure the potential after stabilization. [Note—It may take about 5 min.] The potential difference must be less than 20 mV.

Add 100.0 mL each of *Standard solutions A, B, C,* and *D* to four different 150-mL beakers. To each beaker, add 1 mL of 10 N sodium hydroxide. Place the ammonia electrode in the beaker, stir, and concomitantly measure the potential after stabilization. [Note—It may take about 5 min.] Draw a calibration curve of the potential, in mV, versus, the quantity of ammonium (NH_4^+), in mg.

Add 100.0 mL of the *Sample solution* to a 150-mL beaker. Add 1 mL of 10 N sodium hydroxide. Adjust the pH, if necessary, with 10 N sodium hydroxide to a pH of NLT 11. Place the ammonia electrode in the beaker, stir, and measure the potential after stabilization. [Note—It may take about 5 min.] Obtain the quantity of NH_4^+, in mg, in the 100 mL of the *Sample solution* based on the calibration curve.

Calculate the percentage of ammonium (NH_4^+), in the portion of Racemethionine taken:

$$\text{Result} = (C/W) \times F$$

C = quantity of ammonium in the *Sample solution* from the standard curve (mg)

W = weight of Racemethionine taken to prepare the *Sample solution* (mg)

F = conversion factor to µg/g (ppm), 1×10^6

Acceptance criteria: NMT 200 ppm

Organic Impurities

• **Procedure: Related Substances**

Standard solution A: 0.40 mg/mL of USP Racemethionine RS

Standard solution B: 40 µg/mL of USP Racemethionine RS

Sample solution A: 20 mg/mL of Racemethionine

Sample solution B: 0.40 mg/mL of Racemethionine

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 5 µL

Developing solvent system: Butyl alcohol, glacial acetic acid, and water (3:1:1)

Spray reagent: 2 mg/mL of ninhydrin in a mixture of butyl alcohol and 2 N acetic acid (95:5)

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Sample solution A*, and *Sample solution B*

Develop over a path of 10 cm using the *Developing solvent system*. After air-drying the plate, spray with *Spray reagent*, and heat between 100° and 105° for 15 min. Examine the plate under white light.

Acceptance criteria: Any spot obtained from *Sample solution A*, apart from the principal spot, is not more intense than the spot obtained from *Standard solution B* (NMT 0.2%).

SPECIFIC TESTS

• **pH ⟨791⟩:** 5.4–6.1, in a 20 mg/mL solution

• **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 0.5% of its weight, determined on 1.000 g.

• **Transmittance**

Sample solution: 10% of Racemethionine in 2 N hydrochloric acid, prepared by sonication

Analysis: Determine the transmittance in a 1-cm cell at 430 nm with a suitable spectrophotometer.

Acceptance criteria: Transmittance of NLT 0.98, corresponding to an absorbance of NMT about 0.009

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light.

• **USP Reference Standards ⟨11⟩**

USP Ammonium Chloride RS

USP Racemethionine RS

[1] Orion 95-12 is suitable.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
RACEMETHIONINE	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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